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QUALITY OF LIFE AND PSYCHOSOCIAL FUNCTIONING AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION (ALLO-HSCT) FROM MATCHED SIBLING COMPARED TO UNRELATED DONORS

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Previous studies have shown similar survival outcomes between matched unrelated donor (URD) and matched sibling donor (MSD) transplants. Little data evaluates how this impacts quality of life (QOL) and psychosocial functioning (PF). The purpose of this study was to evaluate and compare QOL between pts undergoing URD vs MSD allo-HSCT.

We prospectively collected QOL and PF assessments in 239 pts who underwent allo-HSCT from 2004-2010 at our single institution. Pts completed three validated psychometric tools—Functional Assessment of Cancer Therapy-Bone Marrow Transplantation (FACT-BMT), Coping Inventory (Brief COPE), and Profile of Mood States Short Form (POMS)—at five time points; (baseline, post-transplant, day 100, 180 and 365). Repeated measures analysis of variance (RMANOVA) and linear mixed model analysis was used to compare QOL scores by donor type and time. Secondary endpoints included overall survival (OS), relapse-free survival (RFS), graft-versus-host-disease (GVHD), and relapse. Outcomes were estimated using Kaplan-Meier and cumulative incidence methods.

Of 239 pts identified, 47 were excluded due to lack of baseline psychometric measurements. Of the remaining 192 pts, 108 received HSCT from URD and 84 from MSD. There were no significant differences in age, race, gender, co-morbidity index, diagnosis, type of transplant (myeloablative vs reduced intensity), and CD34+ dose. There was a difference between time to transplant (7.1 mos for URD vs 5.2 for MSD; $p = 0.014$); preparative regimen ($p = 0.003$); and GVHD prophylaxis ($p<0.001$). Differences were also seen in days until neutrophil (11 vs 16) and platelet (17 vs 23) recovery, as well as length of hospital stay (27 vs 35), ($p<0.001$); with MSD having shorter times as compared with URD. There were no significant differences between baseline QOL and PF between the groups. We saw trends indicating a general decrease in QOL post-discharge with improvement by day 365; but no differences noted between MSD or URD groups. URD transplants had higher Social Well Being scores at day 365 ($p = 0.025$) than MSD, but in no other parameters, and is of unclear significance. With a mean follow up of 33-40 months, there were 43 (40%) URD and 31 (37%) MSD transplant pts alive. There were no significant differences between URD and MSD transplant in regards to GVHD ($p = 0.19$), relapse ($p = 0.09$), OS ($p = 0.96$), or RFS ($p = 0.80$). This study demonstrates that this also correlates with similar QOL and PF between the two groups.

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EARLY READMISSION RATES AFTER AUTOLOGOUS AND ALLOGENEIC HEMATOPOIETIC PROGENITOR CELL TRANSPLANTATION (HPCT)

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Thirty-day readmissions are being targeted as a way to improve cost and quality of medical care. Patients who undergo HPCT often require extensive medical care and frequent hospitalization. It has been demonstrated that readmissions within 30d of a transplant hospitalization are associated with increased mortality. In this study, we retrospectively reviewed all 30d readmissions at our institution in 2010 after an auto or allo-HPCT.

Ninety-nine auto-HPCT were done in 2010, with 11 readmissions. Ten pts (10%) were readmitted after their initial hospitalization within a median time of 4d (range 1-8). Diagnoses included 2 HL, 3 NHL, and 5 MM. One pt was readmitted a second time, 7d after previous hospitalization. The most common reason for readmission was fever/infection (63%). Other reasons included gastrointestinal symptoms (33%) and thromboembolism (11%). There was one death secondary to failure to thrive and subsequent septicemia, occurring 5d after readmission.

There were a total of 62 allo-HPCT done in 2010. Eighteen pts (29%) were readmitted within 30d of their initial transplant hospitalization. Median time to readmission was 9.5d (range 2-30). The majority of these admissions (n = 14, 78%) were within the first 15d of hospital discharge. Diagnosis included 7 AML, 4 ALL, 4 MDS, 1 MF, 1 NHL, and 1 AA. Donor type included 4 UCB, 3 MUD, and 5 MSD. There was no correlation with CIBMTR co-morbidity index scores, which ranged from 0-6. Six (33%) pts were subsequently readmitted at least one more time (range, 2-4 times) within 30d from previous hospitalization. Nine (50%) of the 30d readmissions after allo-HPCT were due to fever/infection, followed by 5 (28%) for GVHD-related symptoms, and 4 (22%) for symptom management (chest pain, nausea/vomiting, diarrhea). There were 3 deaths in this early readmission group, all related to infection or GVHD complications. Median time to death after readmission was 31d (range 27-96).

We previously reported readmissions after HPCT portend poor survival (Mohan et al 2010; Bejanyan et al 2010). The current analysis revealed that these readmissions tended to occur early, within a median time of 4d (for auto) and 10d (for allo). At our institution, we have implemented a review committee that evaluates all 30d readmissions. In addition, we instituted a stringent follow-up policy in which pts are seen within 3d of discharge. Further study of early readmissions may decrease their frequency and improve quality of medical care.

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EVALUATION OF FACTORS ASSOCIATED WITH DAYS OUT OF THE HOSPITAL FOR PATIENTS UNDERGOING UMBILICAL CORD BLOOD TRANSPLANTATION

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Background: Umbilical cord blood transplantation (UCBT) is a feasible option to treat hematologic malignancies in patients lacking a suitably matched conventional donor. However, the median time to hematopoietic recovery after UCBT is prolonged compared to conventional donor transplants, and as a result UCBT patients may spend more time hospitalized for complications in the first 100 days post transplant. We evaluated risk factors associated with prolonged hospitalization in patients undergoing UCBT.

Methods: We performed a retrospective analysis of patients receiving UCBT at the University of Washington (UW) and the Seattle Childrens Hospital (SCH), between January 2006 and April 2011. Fifty-two patients (62%) were conditioned with cyclophosphamide (CY) 60 mg/kg, fludarabine (FLU) 75 mg/m2 and total body irradiation (TBI) 1320 cGy; 19 (23%) with Treosulfan 14 mg/m2, FLU 200 mg/m2 and TBI 200 cGy; and 13 (15%) with CY 50 mg/kg, FLU 200 mg/m2 and either TBI 200 or 300 cGY. GVHD prophylaxis consisted of cyclosporine and MMF. The primary outcome was the number of days alive and out of the hospital within the first 100 days post-transplantation. Linear regression models were used to estimate differences in the primary outcome between patient groups. Variables considered included age, sex, race, institution, disease risk, CMV serostatus, comorbidity score, conditioning regimen, TBI dose and number of donor units.

Results: A total of 84 patients were included in the analysis; 57 (68%) were adult and 27 (32%) pediatric. Nine (11%) patients received a single graft whereas 71 (84%) and 4 (5%) received double and triple grafts, respectively. Fifteen (18%) patients received ex-vivo expanded CD34+ units. Sixty-nine (82%) patients had leukemia, 7 (8%) had a lymphoproliferative disorder, and 8 (10%) had MDS/myeloproliferative disease. Thirteen (15%) patients died in the first 100 days. The median number of days alive and out of the hospital was 54 (range 0-92). In both univariate and multivariable analyses, only transplantation at SCH, non-Caucasian race and high risk disease were significantly associated with fewer days alive and out of hospital [Table 1].

Conclusion: UCBT recipients spent over one-half of the first 100 days after transplant hospitalized; age, race and disease risk were the most important predictors. Future directions for research

include associating these findings with an accurate cost analysis of UCBT.

Table 1. Unadjusted Associations of Transplant Characteristics with Days Alive and Out of Hospital

	N	Median (IQR*)	Coefficient (95% CI)	p-value†
Age				0.16
1-19	26	43 (19-57)	0 (reference)	
20-34	20	52 (23-75)	9.1 (-7.7, 25.8)	
35-49	20	67 (36 – 77)	15.2 (-1.5, 31.9)	
50-73	18	72 (15 -86)	18.2 (0.9, 35.4)	
Institution				0.03
UW Medical Center	57	66 (28 – 79)	0	
Seattle Children's Hospital	27	40 (19 – 57)	-14.9 (-28.1, -1.7)	
Sex				0.21
Female	42	61 (28 – 76)	0	
Male	42	53 (12 – 73)	-8.1 (-20.6, 4.4	
Race				0.002
Caucasian	49	66 (38 – 77)	0	
Non-Caucasian	35	38 (14 – 60)	-19.5 (-31.6, -7.4)	
Disease-Risk				0.02
Standard	74	59 (29 – 76)	0	
High	10	15 (0 – 57)	-22.7 (-41.6, -3.8)	
CMV seropositivity				0.05
Neg	31	66 (40 – 77)	0	
Pos	53	46 (14 – 73)	-12.9 (-25.7, -0.1)	
Comorbidity score (in adults)				0.59
0, 1	14	50 (34 – 64)	0	
2	19	73 (38 – 79)	11.8 (-8.8, 32.4)	
3	14	50 (27 – 66)	-1.1 (-23.3, 21.0)	
4 – 8	15	66 (15 – 83)	5.3 (-16.5, 27.0)	
Conditioning regimen				0.34
CY / Flu / TBI	65	59 (20 – 76)	0	
Treo / Flu / TBI	19	46 (14 – 68)	-7.3 (-22.4, 7.7)	
TBI dose (cGy)				0.46
200 – 300	32	59 (21 – 81)	0	
1320	52	54 (20 – 71)	-4.9 (-17.9, 8.0)	
Number of donors				0.39
1	9	38 (14 – 54)	-10.9 (-31.1, 9.4)	
2	71	59 (27 – 77)	0	
3	4	29 (14 – 58)	-14.8 (-44.2, 14.7)	

*IQR = inter-quartile range, 25th to 75th percentiles of distribution
†Test for homogeneity across factor levels

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BONE MINERAL DENSITY CHANGES IN PATIENTS WITH β-THALASSEMIA MAJOR AFTER HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Introduction: Low bone mineral density (BMD) is an important multifactorial cause of morbidity in patients with β-thalassemia. With recent therapeutic advances such as hematopoietic stem cell transplantation (HSCT), thalassemic patients can live longer but osteoporosis is now a major health concern.
Method: In this study, we evaluated the changes of bone density in 46 patients with β thalassemia major who were candidates for HSCT before and after transplantation. The average age of patients was 13.4 years (range 3-29 years). Twenty four patients (52.2%) were male. All patients underwent HSCT from HLA-identical related donors. Nine patients (19.6%) co-transplanted with mesenchymal cells. Dual-energy X-ray absorptiometry (DXA) was performed on lumbar vertebrae and femoral neck in all patients before starting pre-transplant regimens and repeated at one year after transplantation.
Results: Low BMD was found in 7 patients (15.2%) before transplantation and in 18 patients (39.1%) one year after transplantation. BMD changes in femoral neck and lumbar area were significant at one year after transplant ($p<0.001$) while no significant changes were found in the whole femur ($p = 0.22$). Female gender ($p = 0.005$) and low body mass index ($p = 0.05$) were correlated with low BMD and defined as independent risk factors for low BMD at one year after transplantation. There was no significant difference in BMD changes between patients with and without co-transplantation of mesenchymal cells.
Conclusion: Due to decrease in BMD after HSCT, it is suggested to manage low BMD before transplantation. Longer follow-up will help to better clarify the role of HSCT in BMD changes of thalassemic patients; moreover, further studies are suggested to evaluate the role of co-transplantation of HCT together with mesenchymal cells on BMD improvement of thalassemic patients.

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MEDICATION ERRORS AMONG PEDIATRIC HEMATOPOIETIC STEM CELL TRANSPLANT RECIPIENTS IN AN OUTPATIENT CLINIC

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As care of hematopoietic stem cell transplant (HSCT) patients is increasingly provided in the ambulatory setting a significant amount of responsibility is also switched to family members. The goal of this project was to identify the incidence and source of medication errors in a complex outpatient population and to develop system changes to increase safety and reliability of home administration of medications.

Between 05/11 and 08/11, a prospective study was conducted on pediatric HSCT recipients managed in a hospital-based outpatient clinic. Patients within one year post-transplant or later if still on immunosuppressive therapy were included. Medication reconciliation was performed by a clinic nurse every visit and verified by one of two advanced nurse practitioners (ANP). The latter compared the information with dictated clinic notes to confirm accuracy of medication administration. For variance the ANP determined the source of error and clinical consequence, if any. The results were conferred with the transplant physician for change of management.

Medications were classified as immunosuppressives (IS), anti-infectives (AI) and others (OT). 300 visits (285 allogeneic HSCT- and 15 autologous HSCT) occurred among 49 patients during the 4-month period. 19 medication errors were identified (6% incidence) among 10 patients. 5 patients experienced multiple episodes of error. All were administration errors. 18 errors (95%) occurred at home and one (5%) in the clinic. 18 errors were found in allogeneic patients, 1 in an autologous patient. 7 errors (37%) involved IS, 7 (37%) involved AI, and 5 (26%) from OT. The median time before an error was detected was 2 (range 1-24) days. The median number of drugs taken by each patient was 6 (range 3-14). The nature of the errors was wrong dose (too high 42%, too low 21%) and omission of a dose (7%). The source of the error was traced to miscommunication in 16 events (verbal 16%, written 68%), prescriber error once (5%), and failure of caregiver to refill medication twice (11%). No patient demonstrated significant clinical side-effects from medication errors. Many medications given post HSCT have a narrow therapeutic window. Family members must take responsibility for many skills quickly post HSCT. Standardized dosing strategies and improved communication between the caregivers and healthcare providers may decrease error rate and improve medication adherence and safety of the care delivered.

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EFFECT OF BUSULFAN AND TOTAL BODY IRRADIATION ON DENTAL DEVELOPMENT AFTER HEMATOPOIETIC STEM CELL TRANSPLANTATION IN CHILDHOOD

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Children treated with hematopoietic stem cell transplantation (HSCT) are at particular risk to develop disturbances in dental